

REMARKS

Amendments

The amendments should not be interpreted as an acquiescence to any objection or rejection made in this application, but are made to expedite the prosecution of this application. Claims 1-12 have been amended to place the claims in a format more customary with US practice. The amendments are not intended to and do not limit the scope of equivalents and are not made for purposes of patentability: nor do they change the scope of the claims. Applicants reserve the right to file one or more continuing and/or divisional applications directed to any subject matter disclosed in the application which has been canceled by any of the above amendments.

The Rejection Under 35 U.S.C. §112, Second Paragraph

The rejection of claims 1-13 under 35 U.S.C §112, second paragraph is believed to be rendered moot (in part)by amendments to the claims.

With regards to the phrase “the molecule is identical to naturally occurring epothilone A or B”, naturally occurring epothilones are well known to one skilled in the art and are disclosed within Applicants specification.

Accordingly, it is urged that the present claims are clearly supported by the disclosure and the rejection under 35 U.S.C §112, second paragraph, should be withdrawn.

The Rejection Under 35 U.S.C. - § 112, first paragraph

The rejection of claims 1-13 under 35 U.S.C §112, first paragraph is respectfully traversed.

In the Office Action, claims 1-13 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or to which it is most nearly connected, to make and/or use the invention. The rejection is respectfully traversed.

Applicants specification has provided detailed synthesis information. See for example, page 19 to page 77 and the 35 specific examples. The biological activity and applications of the compounds of the present invention is disclosed for example, at page 78 to page 80 of the specification. Pharmaceutical formulation and dosage amounts are discussed for example, on page 80 line 12 to page 81 line 8. The requirement of teaching how to "make and use" under the statute does not require an applicant to test every possible use of a claimed compound. Also, applicants are not required to provide test results for every species covered by a claim. See, e.g., *In re Angstadt et al.*, 190 USPQ 214, 218 (CCPA 1976).

Applicants respectfully submit that the Office Action fails to meet the burden of proof necessary to properly allege lack of enablement. In order to support a rejection under 35 U.S.C. §112, first paragraph, for lack of enablement, the burden lies first with the Patent and Trademark Office (PTO) to provide evidence or objective reasoning substantiating the allegation that the enabling disclosure is not commensurate in scope with the claims. *In re Marzocchi et al.*, 169 USPQ 367 (CCPA 1971). As stated in Marzocchi,

".. a specification disclosure which contains a teaching of the manner
and process of making and using the invention in terms which
correspond in scope to those used in describing and defining the
subject matter sought to be patented *must* be taken as in compliance

with the enabling requirement of the first paragraph of §112 *unless* there is reason to doubt the objective truth of the statements contained therein..",

and further,

"..it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." (emphasis original).

Further, no specific reasoning is provided in the Office Action to doubt the objective truth of the statements in applicants' disclosure regarding making and using of the compounds having the core structure of Formula I. In the absence of meeting these initial requirements for making a lack of enablement rejection, the rejection under 35 U.S.C. §112, first paragraph, should be withdrawn.

The Rejections Under 35 U.S.C. §102(b) over CA132:293587r and Nicolaou et al.

The rejections under 35 U.S.C. § 102(b), over CA132:293587r and Nicolaou et al. are respectfully traversed.

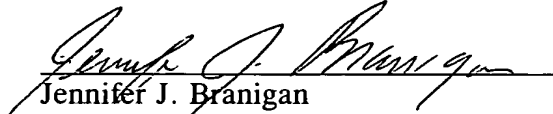
Applicants traverse the rejection on the grounds that a compound meeting all the elements of applicants claims is not specifically identified. The compounds of CA132:293587r and Nicolaou et al. do not exhibit the base structure of the present invention and therefore do not encompass the compounds of the claimed invention. For example, the compounds of CA132:293587r and Nicolaou et al. do not include or suggest materials wherein the R^{2a} or R^{2b} groups are ethyl. Applicants' claims recite that if -D-E- are CH₂-CH₂- and Y=O then R^{2a} and R^{2b} can not be hydrogen or methyl.

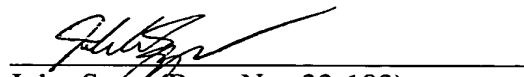
In view of the above remarks, it is respectfully submitted that CA132:293587r and Nicolaou fails to teach Applicants' claimed invention. Withdrawal of the rejection under 35 U.S.C. §102 is respectfully requested.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached pages are captioned **"Version with Markings to Show Changes Made"**.

In view of the above remarks, it is respectfully submitted that the claims of the application are fully supported by the specification and as such are in order for allowance.

Respectfully submitted,


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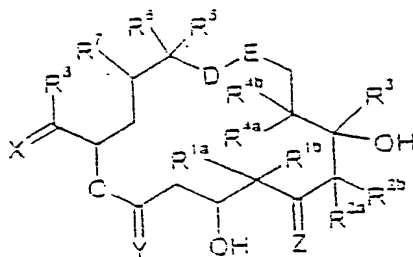
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Name: Jennifer J. Branigan
Signature: [Handwritten Signature]
Date: 27 Feb 03

VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. (Amended) An epoethilone compound ~~Epoethilone derivatives of general formula I,~~



1.

in which

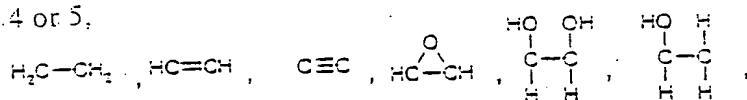
in which
 R^{1a} , R^{1b} are the same or different and mean hydrogen, C_1 - C_{10} alkyl, aryl, C_7 - C_{20} aralkyl, or together a $-(CH_2)_m$ group with $m = 2, 3, 4$ or 5 ,
 R^{2a} , R^{2b} are the same or different and mean hydrogen, C_1 - C_{10} alkyl, aryl, C_7 - C_{20} aralkyl or

R^{2a}, R^{2b} are the same or different and mean hydrogen, C_1 - C_{10} alkyl, aryl, C_7 - C_{20} aralkyl or together a $-(CH_2)_n$ group with $n = 2, 3, 4$ or 5 , whereby, if -D-E- stands for $-CH_2-CH_2-$ or Y stands for an oxygen atom, R^{2a} and R^{2b} cannot be hydrogen or methyl,

$\cdot R^3$ means hydrogen, C_1 - C_{10} alkyl, aryl, C_7 - C_{20} aralkyl,

together a $-(CH_2)_p$ group with $p = 2, 3, 4$ or 5 .

D-E means a group



R³ means hydrogen, C₁-C₁₀ alkyl, aryl, C₇-C₂₀ aralkyl,

R⁶, R⁷ each mean a hydrogen atom, together an additional bond or an oxygen atom,

R³ means hydrogen, C₁-C₂₀ alkyl, aryl, C₇-C₂₀ aralkyl, which can all be substituted,

X means an oxygen atom, two alkoxy groups OR^{11} , a $\text{C}_2\text{--C}_{10}$ alkylene- α,ω -dioxy group, which can be straight-chain or branched, H/OR^9 or a grouping $\text{CR}^{10}\text{R}^{11}$,

whereby

R^{23} stands for a C_1 - C_{20} alkyl radical,

R^9 stands for hydrogen or a protective group PG^9 ,

R^{10} , R^{11} are the same or different and stand for hydrogen, a C_1 - C_{20} alkyl, aryl, C_7 - C_{20} aralkyl radical or R^{10} and R^{11} together with the methylene carbon atom together stand for a 5- to 7-membered carbocyclic ring.

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Y means an oxygen atom or two hydrogen atoms,

Z means an oxygen atom or H/OR¹²,

whereby

R¹² means hydrogen or a protective group PG^z.

2. (Amended) An epothilone compound ~~Epothilone derivatives of general formula I~~ according to claim 1, in which Y, Z, R^{1a}, R^{1b}, R^{2a} and R^{2b} all can have the meanings that are indicated in ~~general~~ formula I, and the remainder of the molecule is identical to naturally occurring epothilone A or B.

3. (Amended) An epothilone compound ~~Epothilone derivatives of general formula I~~ according to claim 1, in which R³, R^{4a}, R^{4b}, D-E, R⁵, R⁶ and R⁷ all can have the meanings that are indicated in ~~general~~ formula I, and the remainder of the molecule is identical to naturally occurring epothilone A or B.

4. (Amended) An epothilone compound ~~Epothilone derivatives of general formula I~~ according to claim 1, in which R⁶, R⁷, R⁸ and X all can have the meanings that are indicated in ~~general~~ formula I, and the remainder of the molecule is identical to naturally occurring epothilone A or B.

5. (Amended) An epothilone compound ~~Epothilone derivatives of general formula I~~ according to claim 1, in which Y, Z, R^{1a}, R^{1b}, R^{2a}, R^{2b}, R³, R^{4a}, R^{4b}, D-E, R⁵, R⁶ and R⁷ all can have the meanings that are indicated in ~~general~~ formula I, and the remainder of the molecule is identical to naturally occurring epothilone A or B.

6. (Amended) An epothilone compound ~~Epothilone derivatives of general formula I~~ according to claim 1, in which Y, Z, R^{1a}, R^{1b}, R^{2a}, R^{2b}, R⁶, R⁷, R⁸ and X all can have the meanings that are indicated in ~~general~~ formula I, and the remainder of the molecule is identical to naturally occurring epothilone A or B.

7. (Amended) An epothilone compound ~~Epothilone derivatives of general formula I~~ according to claim 1, in which R³, R^{4a}, R^{4b}, D-E, R⁵, R⁶, R⁷, R⁸ and X all can have the meanings

that are indicated in ~~general~~ formula I, and the remainder of the molecule is identical to naturally occurring epothilone A or B.

8. ~~(Amended) A compound of~~ Compounds of general formula I, namely

(4S,7R,8S,9S,13(Z),16S(E))-4,8-Dihydroxy-7-ethyl-16-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-1-oxa-5,5,9,13-tetramethyl-cyclohexadec-13-ene-2,6-dione,

(4S,7R,8S,9S,13E,16S(E))-4,8-dihydroxy-7-ethyl-16-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-1-oxa-5,5,9,13-tetramethyl-cyclohexadec-13-ene-2,6-dione (B),

(1S,3S(E),7S,10R,11S,12S,16R)-7,11-Dihydroxy-3-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-10-ethyl-8,8,12,16-tetramethyl-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione,

(1R,3S(E),7S,10R,11S,12S,16S)-7,11-dihydroxy-3-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-10-ethyl-8,8,12,16-tetramethyl-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione,

(1S,3S(E),7S,10R,11S,12S,16S)-7,11-Dihydroxy-3-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-10-ethyl-8,8,12,16-tetramethyl-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione,

(1R,3S(E),7S,10R,11S,12S,16R)-7,11-dihydroxy-3-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-10-ethyl-8,8,12,16-tetramethyl-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione,

(4S,7S,8R,9S,13Z,16S(E))-4,8-Dihydroxy-7-ethyl-16-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-1-oxa-5,5,9,13-tetramethyl-cyclohexadec-13-ene-2,6-dione,

(4S,7S,8R,9S,13E,16S(E))-4,8-dihydroxy-7-ethyl-16-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-1-oxa-5,5,9,13-tetramethyl-cyclohexadec-13-ene-2,6-dione,

(1S,3S(E),7S,10S,11R,12S,16R)-7,11-Dihydroxy-3-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-10-ethyl-8,8,12,16-tetramethyl-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione,

(1R,3S(E),7S,10S,11R,12S,16S)-7,11-dihydroxy-3-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-10-ethyl-8,8,12,16-tetramethyl-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione,

(1S,3S(E),7S,10S,11R,12S,16R)-7,11-Dihydroxy-3-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-10-ethyl-8,8,12,16-tetramethyl-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione,

(1R,3S(E),7S,10S,11R,12S,16S)-7,11-dihydroxy-3-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-10-ethyl-8,8,12,16-tetramethyl-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione,

(4S,7R,8S,9S,13(Z),16S(E))-4,8-Dihydroxy-5,5,7,9,13-pentamethyl-16-((3-pyridyl)ethenyl)-1-oxa-cyclohexadec-13-ene-2,6-dione,

(4S,7R,8S,9S,13E,16S(E))-4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-((3-pyridyl)ethenyl)-1-oxa-cyclohexadec-13-ene-2,6-dione,

(1S,3S(E),7S,10R,11S,12S,16R)-7,11-Dihydroxy-8,8,10,12,16-pentamethyl-3-((3-pyridyl)ethenyl)-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione,

(1S,3S(E),7S,10R,11S,12S,16S)-7,11-dihydroxy-8,8,10,12,16-pentamethyl-3-((3-pyridyl)ethenyl)-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione,

(4S,7R,8S,9S,13(Z),16S(E))-4,8-Dihydroxy-5,5,7,9,13-pentamethyl-16-((4-pyridyl)ethenyl)-1-oxa-cyclohexadec-13-ene-2,6-dione,

(4S,7R,8S,9S,13E,16S(E))-4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-((4-pyridyl)ethenyl)-1-oxa-cyclohexadec-13-ene-2,6-dione,

(1S,3S(E),7S,10R,11S,12S,16R)-7,11-Dihydroxy-8,8,10,12,16-pentamethyl-3-((4-pyridyl)ethenyl)-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione,

(1S,3S(E),7S,10R,11S,12S,16S)-7,11-dihydroxy-8,8,10,12,16-pentamethyl-3-((4-pyridyl)ethenyl)-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione,

(4S,7R,8S,9S,13(E or Z),16S(E))-4,8-Dihydroxy-16-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-1-oxa-7-phenyl-5,5,9,13-tetramethyl-cyclohexadec-13-ene-2,6-dione,

(1(S or R),3S(E),7S,10R,11S,12S,16R)-7,11-Dihydroxy-3-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-10-phenyl-8,8,12,16-tetramethyl-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione,

(1R or S),3S(E),7S,10R,11S,12S,16S)-7,11-Dihydroxy-3-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-10-phenyl-8,8,12,16-tetramethyl-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione,

(4S,7R,8S,9S,13(E or Z),16S(E))-7-Benzyl-4,8-dihydroxy-16-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-1-oxa-5,5,9,13-tetramethyl-cyclohexadec-13-ene-2,6-dione,

(1(S or R),3S(E),7S,10R,11S,12S,16R)-10-Benzyl-7,11-dihydroxy-3-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-8,8,12,16-tetramethyl-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione,

(1R or S),3S(E),7S,10R,11S,12S,16S)-10-Benzyl-7,11-dihydroxy-3-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-8,8,10,12,16-tetramethyl-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione,

(4S,7R,8S,9S,13(E or Z),16S(E))-4,8-Dihydroxy-16-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-1-oxa-5,5,7,13-tetramethyl-9-trifluoromethyl-cyclohexadec-13-ene-2,6-dione,

(1(S or R),3S(E),7S,10R,11S,12S,16R)-7,11-Dihydroxy-3-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-8,8,10,16-tetramethyl-12-trifluoromethyl-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione,

(1R or S),3S(E),7S,10R,11S,12S,16S)-7,11-Dihydroxy-3-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-8,8,10,16-tetramethyl-12-trifluoromethyl-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione,

(4S,7R,8S,9S,11E/Z,13(E or Z),16S(E))-4,8-Dihydroxy-16-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-1-oxa-5,5,7,9,13-pentamethyl-cyclohexadec-11,13-diene-2,6-dione,

(1(S or R),3S(E),7S,10R,11S,12S,14E/Z,16R)-7,11-Dihydroxy-3-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-8,8,10,12,16-pentamethyl-4,17-dioxabicyclo[14.1.0]heptadec-14-ene-5,9-dione,

(1R or S),3S(E),7S,10R,11S,12S,14E/Z,16S)-7,11-Dihydroxy-3-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-8,8,10,12,16-pentamethyl-4,17-dioxabicyclo[14.1.0]heptadec-14-ene-5,9-dione,

(4S,7R,8S,9S,13(E or Z),16S(E))-4,8-Dihydroxy-16-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-1-oxa-5,5,7,9,13-pentamethyl-cyclohexadec-13-ene-11-ene-2,6-dione

(1(S or R),3S(E),7S,10R,11S,12S,16R)-7,11-Dihydroxy-3-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-8,8,10,12,16-pentamethyl-4,17-dioxabicyclo[14.1.0]heptadec-14-ene-5,9-dione

(1R or S),3S(E),7S,10R,11S,12S,16S)-7,11-Dihydroxy-3-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-8,8,10,12,16-pentamethyl-4,17-dioxabicyclo[14.1.0]heptadec-14-ene-5,9-dione

(4S,7R,8S,9S,13(E or Z),16S(E))-4,8-Dihydroxy-16-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-1-oxa-5,5,7,9-tetramethyl-13-trifluoromethyl-cyclohexadec-13-ene-2,6-dione,

(1(S or R),3S(E),7S,10R,11S,12S,16R)-7,11-Dihydroxy-3-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-8,8,10,12-tetramethyl-16-trifluoromethyl-4,17-dioxabicyclo[14.1.0]heptadeca-5,9-dione,

(1R or S),3S(E),7S,10R,11S,12S,16S)-7,11-Dihydroxy-3-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-8,8,10,12-tetramethyl-16-trifluoromethyl-4,17-dioxabicyclo[14.1.0]heptadeca-5,9-dione,

(4S,7R,8S,9S,13(E or Z),16S(E))-4,8-Dihydroxy-16-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-1-oxa-13-pentafluoroethyl-5,5,7,9-tetramethyl-cyclohexadec-13-ene-2,6-dione,

(1(S or R),3S(E),7S,10R,11S,12S,16R)-7,11-Dihydroxy-3-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-16-pentafluoroethyl-8,8,10,12-tetramethyl-4,17-dioxabicyclo[14.1.0]heptadeca-5,9-dione,

(1R or S),3S(E),7S,10R,11S,12S,16S)-7,11-Dihydroxy-3-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-16-pentafluoroethyl-8,8,10,12-tetramethyl-4,17-dioxabicyclo[14.1.0]heptadeca-5,9-dione,

(4S,7R,8S,9S,13(E or Z),16S(E))-4,8-Dihydroxy-16-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-1-oxa-5,5-(1,3-trimethylene)-7,9,13-trimethyl-cyclohexadec-13-ene-2,6-dione,

(1(S or R),3S(E),7S,10R,11S,12S,16R)-7,11-Dihydroxy-3-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-8,8-(1,3-trimethylene)-10,12,16-trimethyl-4,17-dioxabicyclo[14.1.0]heptadeca-5,9-dione,

(1R or S),3S(E),7S,10R,11S,12S,16S)-7,11-Dihydroxy-3-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-8,8-(1,3-trimethylene)-10,12,16-trimethyl-4,17-dioxabicyclo[14.1.0]heptadeca-5,9-dione,

(4S,7R,8S,9S,11E/Z,13(E or Z),16S(E))-4,8-Dihydroxy-13-ethyl-16-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-1-oxa-5,5,7,9-tetramethyl-cyclohexadec-11,13-diene-2,6-dione,

(1(S or R),3S(E),7S,10R,11S,12S,14E/Z,16R)-7,11-Dihydroxy-16-ethyl-3-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-8,8,10,12-tetramethyl-4,17-dioxabicyclo[14.1.0]heptadec-14-ene-5,9-dione,

(1R or S),3S(E),7S,10R,11S,12S,14E/Z,16S)-7,11-Dihydroxy-16-ethyl-3-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-8,8,10,12-tetramethyl-4,17-dioxabicyclo[14.1.0]heptadec-14-ene-5,9-dione,

(4S,7R,8S,9S,11E/Z,13(E or Z),16S(E))-4,8-Dihydroxy-16-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-1-oxa-13-propyl-5,5,7,9-tetramethyl-cyclohexadec-11,13-diene-2,6-dione,

(1(S or R),3S(E),7S,10R,11S,12S,14E/Z,16R)-7,11-Dihydroxy-3-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-16-propyl-8,8,10,12-tetramethyl-4,17-dioxabicyclo[14.1.0]heptadec-14-ene-5,9-dione,

(1R or S),3S(E),7S,10R,11S,12S,14E/Z,16S)-7,11-Dihydroxy-3-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-16-propyl-8,8,10,12-tetramethyl-4,17-dioxabicyclo[14.1.0]heptadec-14-ene-5,9-dione,

(4S,7R,8S,9S,13(E or Z),16S(E))-4,8-Dihydroxy-16-(1-methyl-2-(2-pyridyl)ethenyl)-1-oxa-5,5,7,9,13-pentamethyl-cyclohexadec-13-ene-2,6-dione,

(1(S or R),3S(E),7S,10R,11S,12S,16R)-7,11-Dihydroxy-3-(1-methyl-2-(2-pyridyl)ethenyl)-8,8,10,12,16-pentamethyl-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione,

(1R or S),3S(E),7S,10R,11S,12S,16S)-7,11-Dihydroxy-3-(1-methyl-2-(2-pyridyl)ethenyl)-8,8,10,12,16-pentamethyl-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione,

(4S,7R,8S,9S,13(E or Z),16S(E))-4,8-Dihydroxy-16-(1-methyl-2-(4-pyridyl)ethenyl)-1-oxa-5,5,7,9,13-pentamethyl-cyclohexadec-13-ene-2,6-dione,

(1(S or R),3S(E),7S,10R,11S,12S,16R)-7,11-Dihydroxy-3-(1-methyl-2-(4-pyridyl)ethenyl)-8,8,10,12,16-pentamethyl-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione,

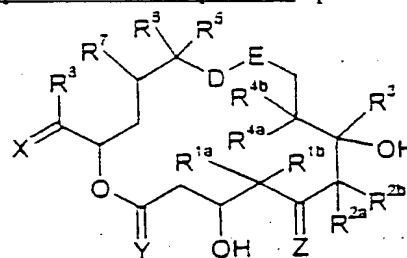
(1® or S),3S(E),7S,10R,11S,12S,16S)-7,11-Dihydroxy-3-(1-methyl-2-(4-pyridyl)ethenyl)-8,8,10,12,16-pentamethyl-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione,

(4S,7R,8S,9S,13(E or Z),16S(E))-4,8-Dihydroxy-16-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-5,5,7,9,13-pentamethyl-cyclohexadec-13-en-6-one,

(1(S or R),3S(E),7S,10R,11S,12S,16R)-7,11-Dihydroxy-3-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-8,8,10,12,16-pentamethyl-4,17-dioxabicyclo[14.1.0]heptadec-9-one,

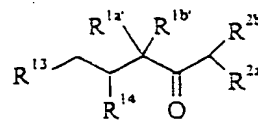
(1R or S),3S(E),7S,10R,11S,12S,16S)-7,11-Dihydroxy-3-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-8,8,10,12,16-pentamethyl-4,17-dioxabicyclo[14.1.0]heptadec-9-one.

9. (Amended) Process for the production of an epothilone compound Epothilone derivatives of general formula I according to claim 1



in which

I,
the substituents have the meanings that are indicated in general formula I,
~~characterized in that~~ wherein a fragment of general formula A



in which

$R^{1a'}$, $R^{1b'}$, $R^{2a'}$ and $R^{2b'}$ have the meanings already mentioned for R^{1a} , R^{1b} , R^{2a} and R^{2b} ,

R^1 means $\text{CH}_2\text{OR}^{13a}$, $\text{CH}_2\text{-Hal}$, CHO , $\text{CO}_2\text{R}^{13b}$, COHal ,

R^1 means hydrogen, OR^{14a} , Hal , $\text{OSO}_2\text{R}^{14b}$,

R^{13a} , R^{14a} mean hydrogen, $\text{SO}_2\text{-alkyl}$, $\text{SO}_2\text{-aryl}$, $\text{SO}_2\text{-aralkyl}$ or together a $-(\text{CH}_2)_o$ group

or together a $CR^{15a}R^{15b}$ group,

R^{13b} , R^{14b} mean hydrogen, C_1 - C_{20} alkyl, aryl, C_1 - C_{20} aralkyl,

R^{15a} , R^{15b} are the same or different and mean hydrogen, C_1 - C_{10} alkyl, aryl, C_7 - C_{20} aralkyl

or together a $-(CH_2)_q$ group,

Hal means halogen,

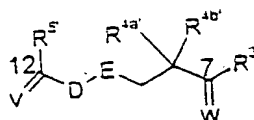
o means 2 to 4,

q means 3 to 6,

including all stereoisomers as well as their mixtures, and

free hydroxyl groups in R^{13} and R^{14} can be etherified or esterified, free carbonyl groups can be ketalized in A and R^{13} , converted into an enol ether or reduced, and free acid groups in A can be converted into their salts with bases,

is reacted with a fragment of general formula B



B

in which

R^3 , R^{4a} , R^{4b} and R^5 have the meanings already mentioned for R^3 , R^{4a} , R^{4b} and R^5 ,

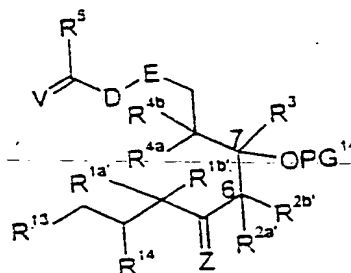
V means an oxygen atom, two alkoxy groups OR^{17} , a C_2 - C_{10} alkylene- α,ω -dioxy group, which can be straight-chain or branched or H/OR^{16} ,

W means an oxygen atom, two alkoxy groups OR^{19} , a C_2 - C_{10} alkylene- α,ω -dioxy group, which can be straight-chain or branched or H/OR^{18} ,

R^{16} , R^{18} , independently of one another, mean hydrogen or a protective group PG^1

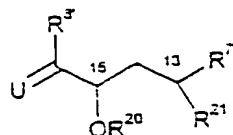
R^{17} , R^{19} , independently of one another, mean C_1 - C_{20} alkyl,

to a partial fragment of general formula AB



AB,

in which $R^{1a'}$, $R^{1b'}$, $R^{2a'}$, $R^{2b'}$, R^3 , R^{4a} , R^{4b} , R^5 , R^{13} , R^{14} , D, E, V and Z have the meanings already mentioned, and PG^{14} represents a hydrogen atom or a protective group PG , and this partial fragment AB is reacted with a fragment of general formula C



in which

C

R^8 has the meaning already mentioned in general formula I for R^8 , and

R^7 means a hydrogen atom,

R^{20} means a hydrogen atom or a protective group PG^2 ,

R^{21} means a hydroxy group, halogen, a protected hydroxy group OPG^3 , a phosphonium halide radical $PPh_3^+Hal^-$ (Ph = phenyl; Hal = F, Cl, Br, I), a phosphonate radical $P(O)(OQ)_2$ (Q = C_1 - C_{10} alkyl or phenyl) or a phosphine oxide radical $P(O)Ph_2$ (Ph = phenyl),

U means an oxygen atom, two alkoxy groups OR^{23} , a C_2 - C_{10} alkylene- α,ω -dioxy group, which can be straight-chain or branched, H/OR^9 or a grouping $CR^{10}R^{11}$,

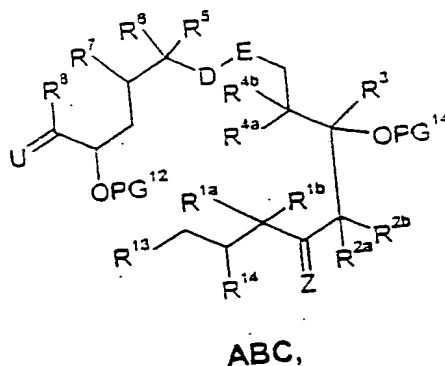
whereby

R^{23} stands for a C_1 - C_{20} alkyl radical,

R^9 stands for hydrogen or a protective group PG^3 ,

R^{10} , R^{11} are the same or different and stand for hydrogen, a C_1 - C_{20} alkyl, aryl, C_7 - C_{20} aralkyl radical or R^{10} and R^{11} together with the methylene carbon atoms together stand for a 5- to 7-membered carbocyclic ring,

to a partial fragment of general formula ABC



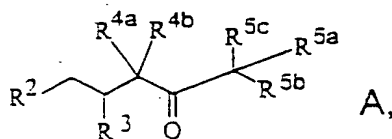
ABC,

in which $R^{1a'}$, $R^{1b'}$, $R^{2a'}$, $R^{2b'}$, R^3 , R^{4a} , R^{4b} , R^5 , R^6 , R^7 , R^8 , R^{13} , R^{14} , D, E, U and Z have the meanings already mentioned, and this partial fragment of general formula ABC is cyclized to an epothilone derivative of general formula I.

10. (Amended) A pharmaceutical composition ~~Pharmaceutical preparations that contain~~ comprising at least one compound of general formula I according to claim 1, as well as a pharmaceutically compatible vehicle.

11. (Amended) A method for the production of pharmaceutical agents comprising mixing a compound ~~Use of the compounds of general~~ of formula I according to claim 1, ~~for the production of pharmaceutical agents together with a pharmaceutically compatible vehicle.~~

12. (Amended) A process for the production of a compound of ~~compounds of~~ general formula A



in which

R^2 means CH_2OR^{2a} , CHO , CO_2R^{2b} , COX ,

R^{2a} , R^{2b} mean hydrogen, C_1 - C_{20} alkyl, aryl, C_7 - C_{20} aralkyl,

R^3 means hydrogen, OR^{3a} , X , OSO_2R^{3b} ,

R^{3a} means hydrogen or together with R^{2a} a $-(CH_2)_n$ group or a $CR^{6a}R^{6b}$ group,

R^{3b} means C_1 - C_4 alkyl, aryl,

X means halogen,

n means 2 to 4,

R^{6a} , R^{6b} are the same or different and mean C_1 - C_8 alkyl, C_6 - C_{10} aryl or together a -

$(CH_2)_o$ group,

o means 3 to 6,

R^{6a} additionally can assume the meaning of hydrogen,

R^{4a} , R^{4b} are the same or different and mean hydrogen, C_1 - C_{10} alkyl, C_7 - C_{20} aralkyl

or together a $-(CH_2)_m$ group,

m means 2 to 5

R^{5a} , R^{5b} are the same or different and mean hydrogen, C_1 - C_{10} alkyl, C_7 - C_{20} aralkyl

or together a $-(CH_2)_p$ group,

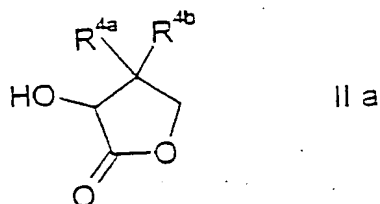
p means 2 to 5

R^{5c} means hydrogen,

including all stereoisomers and mixtures thereof, and

free hydroxyl groups can be etherified or esterified in R^2 and R^3 , free carbonyl groups can be ketalized in A and R^2 , converted into an enol ether or reduced, and free acid groups in A can be converted into their salts with bases, wherein

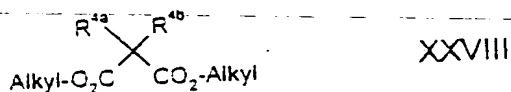
a) a pantolactone of general formula IIa or



in which

R^{4a} and R^{4b} in each case are methyl groups or

b) a malonic acid dialkyl ester of general formula XXVIII



in which

R^{4a} , R^{4b} , which have the meaning that is indicated in general formula A, and alkyl, independently of one another, mean a C_1 - C_{20} alkyl, C_3 - C_{10} cycloalkyl or C_4 - C_{20} alkylcycloalkyl radical, is used as a starting product.